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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,677	01/07/2005	Akira Yanagawa	264232US0PCT	9965

22850 7590 09/05/2008

OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER
ALSTRUM ACEVEDO, JAMES HENRY

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
09/05/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/519,677	YANAGAWA, AKIRA	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 11-20 are pending. Applicant previously cancelled claims 1-10 and claims 21-22. Applicant amended claim 11. Receipt and consideration of Applicant's amended claim set and remarks/arguments submitted on June 9, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments and/or persuasive arguments. Applicant's claim amendments have necessitated a new ground of rejection (i.e. under 35 USC §112, 1st paragraph, new matter).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement (new matter). The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has amended independent claim 11 to recite a carrier average particle size range of 60 microns to 100 microns and has alleged that support for this claimed range is found in the original claims and throughout the specification. Applicant did not point to any particular page and line number where support was allegedly found. A review of the original claims and the specification did not uncover any explicit support for an average carrier particle size of 60 microns to 100 microns. In general, for a numerical range to have written

support it must be explicitly recited either in the original claims or the specification, however, this is not the case here. Applicant's original claims and specification only provide support for the following carrier average particle size ranges: (a) 500 microns or less (e.g. original claim 1), (b) 20 to 100 microns (e.g. original claim 6), (c) less than or up to 250 microns (pg. 11 of Applicant's specification), and about 62 microns (pg. 17 of Applicant's specification). The broader ranges do not provide sufficient written description for a narrower range contained therein. Thus, Applicant's claim amendment introduces new matter.

The remaining claims are rejected as depending from a rejected claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-20 **remain rejected** under 35 U.S.C. 103(a) as being unpatentable over Yanagawa (U.S. Patent No. 5,603,943) ("USPN '943") in view of Wermeling (US 2003/0077300) and the 1999-2000 Drug Information Handbook ("DIH") (Lacy, C. F.; Armstrong, L.L.; Goldman, M. P.; Lance, L. L., Lexi-Comp, Inc: Hudson, OH, 1999, pp 349-350 and 414-417) for the reasons of record restated below.

Applicant Claims

Applicant claims (1) a composition for nasal absorption comprising a carrier of calcium carbonate and/or calcium phosphate having an average particle size of 60-100 microns an effective dose of an opioid analgesic selected from the group consisting of fentanyl, fentanyl citrate, and a droperidol/fentanyl citrate preparation and (2) a method of treating post surgery or cancer pain comprising intranasally administering said composition.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Yanagawa were set forth on pages 4-5 of the office action mailed on June 15, 2006 and are restated herein.

Yanagawa discloses in claims 1-2, 4, and 9-14:

1. A nasally administrable composition comprising a physiologically active substance having a molecular weight of not more than 40,000 and a physiologically acceptable powdery or crystalline polyvalence metal carrier, wherein a physiologically effective amount of said physiologically active substance is dispersed homogeneously in and adsorbed homogeneously onto said polyvalence metal carrier, and a mean particle size of said polyvalence metal carrier is not more than 250 μm.

2. A nasally administrable composition as claimed in claim 1, wherein said polyvalence metal carrier is divalence metal compound selected from the group consisting of aluminum compound, calcium compound, magnesium compound, silicon compound, iron compound and zinc compound.

4. A nasally administrable composition as claimed in claim 2, wherein said calcium compound is selected from the group consisting of apatite, hydroxyapatite, calcium carbonate, calcium disodium EDTA, calcium chloride, calcium citrate, calcium glycerophosphate, calcium gluconate, calcium silicate, calcium oxide, calcium hydroxide, calcium stearate, calcium phosphate tribasic, calcium lactate, calcium pantothenate, calcium oleate, calcium palmitate, calcium D-pantothenate, calcium alginate, calcium phosphate anhydride, calcium hydrogenphosphate, calcium primary phosphate, calcium acetate, calcium saccharate, calcium sulfate, calcium secondary phosphate, calcium para-aminosalicylate, and bio calciutite compounds.

9. A nasally administrable composition as claimed in claim 4, wherein said calcium compound is hydroxyapatite, calcium carbonate or calcium lactate.

10. A nasally administrable composition as claimed in claim 5, wherein said magnesium compound is magnesium stearate.

11. A nasally administrable composition as claimed in claim 3, wherein said aluminum compound is aluminum hydroxide.

12. A nasally administrable composition as claimed in claim 1, wherein said polyvalence metal carrier has a mean partice size of not more than 100 μm.

13. A nasally administrable composition as claimed in claim 12, wherein a mean particle size of said polyvalence metal carrier ranges from 30 μm to 60 μm.

14. A nasally administrable composition as claimed in claim 1, wherein the physiologically active substance having a molecular weight of not more than 40,000 is any one of compound selected from the group consisting of physiologically active peptide, hypnotics and sedatives, anti-epileptics,

Yanagawa teaches that the physiologically acceptable substances that may be used with the nasally administrable inorganic carriers may be any that has a molecular weight less than 40,000 such as those that are employed as ordinary pharmaceuticals, for example, **antiemetics** (col. 4, lines 28-44).

DIH teaches that **droperidol is a known antiemetic (i.e. anti-nausea drug)** (pp 349). DIH teaches that **fentanyl and fentanyl citrate are known opioid analgesics that *may cause nausea*** and other side effects (pp 414). DIH teaches that **the preparation of droperidol/fentanyl is known** and sold under the trademark name of INNOVAR® (pp 350).

Wermeling teaches a system and method for **intranasal administration of opioids, including fentanyl** (title; abstract; [0022]; [0129]; claims 15 and 20). Wermeling's formulations are in the form of liquids [0129].

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Yanagawa lacks the express teaching of compositions wherein the active substance is selected from the group consisting of fentanyl and fentanyl citrate. This deficiency is cured by the teachings of the DIH. Wermeling is provided as a supporting reference to demonstrate that the nasal delivery of opioids, such as fentanyl, was known at the time of the instant invention.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art to utilize and opioid analgesic as the active substance in Yanagawa's compositions, because Yanagawa teaches that suitable active substances are those with a molecular weight below 40,000 that are employed as ordinary pharmaceuticals. It is clearly evident from the teachings of the DIH, that fentanyl; opioid analgesics in general, are ordinarily employed as pharmaceuticals. Thus, an ordinary skilled artisan would have been motivated to utilize an opioid analgesic in Yanagawa's compositions. At the very least, the incorporation of a conventional opioid analgesic into Yanagawa's compositions would have been obvious to try, because opioids are ordinarily employed pharmaceuticals; are known to be nasally administrable (Wermeling), and thus the ordinary skilled artisan would have had a reasonable expectation of predictably of successfully administering an opioid analgesic (e.g. fentanyl) using Yanagawa's modified composition. An ordinary skilled artisan would have had a reasonable expectation of success upon modification of the teachings of Yanagawa to utilize an opioid analgesic, selected from fentanyl and fentanyl citrate; because it is well known that opioids are nasally administrable (Wermeling).

Furthermore, fentanyl and fentanyl citrate all meet the indicated molecular weight requirement taught by Yanagawa and all these drugs are also ordinarily employed as pharmaceuticals. Regarding the carrier particle size, the range taught by Yanagawa encompasses Applicant's recited carrier average particle size range. Thus, optimization of the range disclosed by Yanagawa would necessarily result in the range recited by Applicant. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments filed June 9, 2008, have been fully considered but they are not persuasive. Applicant's traversal is based on the assertion that there is allegedly no motivation to combine the cited references because there is no nexus between the cited references that would result in Applicant's claimed formulation.

The Examiner respectfully disagrees. Yanagawa's disclosure provides clear guidance that pharmaceuticals with a molecular weight below 40,000 g/mol are suitable for incorporation in Yanagawa's invented nasal formulations. Furthermore, Yanagawa indicates that any drug that is ordinarily utilized as a pharmaceutical and meets the molecular weight requirement is suitable, as evidence by the wide variety of drug classes recited in Yanagawa's claim 14. In addition, as evidenced by Wermeling, opioids are known to be nasally administrable. Thus, the prior art recognizes that opioids may be administered via the nasal mucosa and that Yanagawa's invented nasal carrier compositions are suitable for use with any pharmaceutical with a molecular weight

less than 40,000 g/mol. It is also noted that Applicant's claims utilize open, "comprising" claim language and do not exclude the presence of other active agents or the combination of opioids with anti-emetics. Thus, for the reasons set forth above, there is motivation to combine the cited references. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 11-20 are rejected as being unpatentable over claims 1-2, 4, and 9-14 of U.S. Patent No. 5,603,943 (USPN '943) in view of Wermeling (US 2003/0077300) and the 1999-2000 Drug Information Handbook ("DIH") (Lacy, C. F.; Armstrong, L.L.; Goldman, M.

P.; Lance, L. L., Lexi-Comp, Inc: Hudson, OH, 1999, pp 349-350 and 414-417) for the reasons of record set forth on pages 7-8 of the office action mailed on June 15, 2006 and set forth above in the instant office action.

Applicant's claims have been described above as have the teachings of the DIH and Wermeling. The claims of Yanagawa were described in the office action mailed on June 15, 2006. The difference between Applicant's claims and those of Yanagawa is that the claims of USPN '943 do not recite compositions comprising fentanyl, fentanyl citrate, or a droperidol/fentanyl citrate preparation as the physiologically active substance. This deficiency is cured by the teachings of Wermeling and the DIH, set forth above in the instant office action. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 11-20 *prima facie* obvious over claims 1-2, 4, and 9-14 of U.S. Patent No. 5,603,943 (USPN '943) in view of Wermeling (US 2003/0077300) and the 1999-2000 Drug Information Handbook ("DIH") (Lacy, C. F.; Armstrong, L.L.; Goldman, M. P.; Lance, L. L., Lexi-Comp, Inc: Hudson, OH, 1999, pp 349-350 and 414-417).

Response to Arguments

Applicant's arguments filed June 9, 2008, have been fully considered but they are not persuasive. Applicant's traversal is based on the same arguments traversing the above rejection under 35 USC §103(a). The Office's rebuttal of these arguments is herein incorporated by reference and the rejection is maintained.

Conclusion

Claims 11-20 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.H.A.-A.
Patent Examiner
Technology Center 1600

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616